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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,377	09/14/2006	Alastair David Griffiths Lawson	13001012PCTUS	1120

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EXAMINER	
SAUNDERS, DAVID A	
ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
12/18/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,377	LAWSON ET AL.	
	Examiner	Art Unit	
	David A. Saunders	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7 and 19* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

AMENDMENT ENTRY

Amendment of 9/14/09 has been entered. Claims 1-7 and 19 are pending and are under examination.

NEW REJECTION(S) UNDER 35 USC 112, SECOND PARAGRAPH

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

If the "antigen of part ii) is present on the surface of a cell", as in claim 5, then it is meaningless to state that this antigen is "at a concentration of 1uM to 1pM", as required by base claim 1. Any antigen that is "present on the surface of a cell" is present on particulate matter, it is thus meaningless to its concentration in any sort of Molarity, as one would for a truly soluble antigen.

NEW REJECTION(S) UNDER 35 USC 112, FIRST PARAGRAPH

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As noted supra under 35 USC 112, second para., it is meaningless to state that an antigen that is "present on the surface of a cell" antigen is present "at a concentration of 1uM to 1pM", as required by base claim 1. One of skill would not know how to provide this cell surface antigen at a concentration of 1um to 1pM, in order to practice step a) of base claim 1, because any sort of Molar concentration could only be calculated for a truly soluble antigen and not for an antigen that is present on the surface of cellular/particulate matter.

MAINTAINED REJECTION(S) UNDER 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Irsch et al (5,786,161, cited on PTO-1449) in light of Lazdunski et al (6,875,599, newly cited on PTO-892) as an evidentiary reference.

Irsch et al teach a method of isolating B-cells which produce an antibody which recognizes an allergen/antigen; see disclosure of B-cells at col. 4, lines 9-11. A population of B-cells is contacted with an allergen coupled to a hapten, and these are incubated so that allergen can bind to cell surface bound antibody/immunoglobulin (Ig); see col. 6, lines 7-17. The thus incubated cells are then contacted with avidin coated magnetic particles, to which a biotinylated anti-hapten antibody has been complexed. See col. 6, lines 19-23. This second binding step forms a sandwich complex of:

B-cells --- hapten-antigen --- biotinylated-antibodies-avidin-beads.

From these teachings instant claim 1 is anticipated, particularly for the order of contacting set forth in dependent claim 3.

Clearly, dependent claim 6 is anticipated, since Irsch et al teach magnetic separation; see col. 6, lines 22-23 and col. 6, line 49-col. 7, line 34.

The above stated rejection is proper, since nothing in the claim language rules out the use of an antigen coupled to another moiety, such as a hapten.

Applicant's arguments filed 9/14/09 have been fully considered but they are not persuasive. Applicant has urged that Irsch et al do not teach that the antigen is provided at a concentration of 1uM to 1pM, as recited in amended claim 1. However, the Office finds that the taught concentration of the allergen (i.e. antigen) digoxigenin conjugate was 10 ug/ml (para. spanning cols. 8-9). The Office considers that the phospholipase A2 allergen from bee venom used by Irsch et al inherently has a m.w. of ~14,600. Evidence for this m.w. comes from Lazdunski et al, who show that the phospholipase A2 allergen from bee venom has 133 amino acid residues. See SEQ ID NO:6 in Fig. 2 and in the SEQ ID listing. If one takes 110 as the av. m.w. of an amino acid residue, then the phospholipase A2 allergen has an estimated m.w. of 133 x 110 = ~14,600. The reference does not disclose the actual number of digoxignein hapten moieties conjugated to each allergen; thus the Office shall conservatively round the m.w. of 14,600 up to 15,000, in order to account for the increased m.w. due to the presence of the conjugated digoxignein hapten moieties.

The 10 ug/ml of allergen used by Irsch et al converts to a conc. of 10 mg/L.

The 10 mg of allergen present in 1 L thus constitutes:

10 mg/L over 15,000 g/mol = 10^{-2} g/L over 1.5×10^{4} g/mol

$= 0.67 \times 10^{-6}$ mol/L = 0.67 umol/L = 0.67 uM.

The Office thus finds that the taught concentration of the allergen digoxigenin conjugate of 10 ug/ml is inherently a concentration of ~ 0.67 uM (The estimated uM concentration would be lowered even further, if one were to assume a higher degree of conjugation of the digoxignein hapten moieties, so that the m.w. of the conjugate would be even higher than 15,000). All limitations of amended claim 1 are thus met by the reference, and the rejection is properly maintained.

REJECTION(S) UNDER 35 USC 102/103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 7 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Irsch et al alone or in view of Steenbakkers (EP 0,448,470, A1, Cited on PTO-892).

Irsch et al have been cited above for showing the steps of claim 1, in which B-cells that produce an antibody that recognizes an antigen are isolated. Irsch et al give hints that one might want to immortalize the selected cells, in order to produce antibodies (e.g. col. 4, lines 9-22; col. 8, lines 12-22). Irsch et al do not point out all of the steps involved in such production of antibodies from the immortalized cells. However, Steenbakkers teaches one how to isolate individual B-cell or a population of B-cells that produce an antibody that recognizes an antigen. Among the methods for isolating such antigen-specific B-cells are those involving the use of magnetic/paramagnetic beads (p 4, lines 10-14). Thus one practicing the methods of Steenbakkers would have found it obvious to have connected the teachings of Steenbakkers with the cell isolation methods of Irsch et al. Steenbakkers further teaches that such isolated B-cells that produce an antibody that recognizes an antigen can be cultured (i.e subjected to clonal expansion, immortalized, further cultured, and used to produce antibodies (e.g. p 3, lines 35-40). Note teachings of screening cultures for production of a specific antibody (e.g. Tables at pp 9-14). Thus the further steps of

culturing, screening and isolating an antibody from the B-cells selected by the method of Irsch et al would have been obvious.

This rejection of record has been maintained since, just as the new antigen concentration limitations of claim 1 are inherent to the teachings of Irsch et al, the new antigen concentration limitations of claim 7 are also inherent to the teachings of Irsch et al.

Claims 1, 3-4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Irsch et al in view of Brown et al (WO 04/051268, cited in IDS of 6/5/06).

Reliance upon Brown et al (WO 04/051268) is proper under 102(e), since the instant record has not established that Brown et al (WO 2004/051268) and the instant inventors were subject to common assignment at the time both of the inventions were made. Furthermore, citation of Brown et al (WO 2004/051268) is proper because applicant cannot claim benefit of the earliest GB priority date of 20 Aug 2003 (priority document 0319587.2 only shows the "homogenous" assay of Brown et al (WO 04/051268) and does not show the instant-non-homogenous/ heterogenous assay). Therefore the International Filing Date of 01 Dec 2003 for WO 2004/051268 renders this reference effective under 102(e).

Irsch et al have been cited supra for showing a method in which the "antigen of interest" carries a hapten, and in which the particle bears an anti-hapten antibody. Brown et al show a method in which one, likewise, forms a complex in which antigen recognized by an antibody becomes indirectly bound to a particle; this antigen bearing particle is employed in a method of binding antigen-specific B-cells. In the case of Brown et al, the complex is formed between antigen, not coupled to anything, and a particle-immobilized polyclonal antibody that recognizes the antigen. See p 8, lines 11-29. One of ordinary skill would have recognized that the method of Irsch et al, in which one forms a complex consisting of antigen-hapten and anti-hapten, and the method of Brown et al, in which one forms a complex consisting of antigen and anti-antigen antibody are equivalent ways of indirectly providing a particle bearing an antigen which can be recognized by antigen specific B-cells. Even though the methods of Irsch et al

and Brown et al may differ in the way they use the particles (i.e. the former teach a "heterogeneous" method involving separation step(s) and the latter teach a "homogeneous" method involving no separation step), the particles in each case are of the same nature. Thus, whether then antigen is indirectly bound to a particle via hapten-anti-hapten binding (as in Irsch et al) or via antigen-anti-antigen binding (as in Brown et al) makes no difference as to whether the particles could be used in one of the taught methods or the other. Therefore it would have been obvious to use particles with antigen indirectly coupled via antigen-anti-antigen binding (as in Brown et al) in the cell B-cell isolation method of Irsch et al. Thus instant claim 1, would have been obvious.

Instant claim 3 would have been obvious, if one were to consider following the order of addition of components as taught by Irsch et al.

Instant claim 4 would have been obvious, if one were to consider following the order of addition of components as taught by Brown et al (e.g. p 8, lines 23-19).

Regarding claim 6, Brown et al teach that the particles can be magnetic (p 8, line 9).

This rejection of record has been maintained since the new antigen concentration limitations of claim 1 are inherent to the teachings of Irsch et al.

Claims 7 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Irsch et al in view of Brown et al and further in view of Steenbakkers et al.

Irsch et al and Brown et al have been cited above for showing that the steps of claim 1, in which B-cells that produce an antibody that recognizes an antigen are isolated, would have been obvious. Irsch et al give hints that one might want to immortalize the selected cells, in order to produce antibodies (e.g. col. 4, lines 9-22; col. 8, lines 12-22). Irsch et al do not point out all of the steps involved in such production of antibodies from the immortalized cells. However, Steenbakkers teaches that one can isolate individual B-cell or a population of B-cells that produce an antibody that recognizes an antigen and then, further, that one can culture (clonally expand), immortalize, further culture, and use the cells to produce antibodies (p 3, lines 35-40).

The rational for reliance upon the further teachings of Steenbakkers follows that set forth supra, in the rejection over Irsch et al in view of Steenbakkers.

This rejection of record has been maintained since the new antigen concentration limitations of claim 1 are inherent to the teachings of Irsch et al.

CLAIM(S) OBJECTED TO

Claim 2 is listed as objected to on Form PTOL-326. The limitations of claim 2 are not shown by Irsch et al. While one might have realized, by hindsight, that the contacting of parts i)-iii) could be conducted "simultaneously", Irsch et al do not point one in this direction. They more specifically refer to a "first binding step" followed by a "second binding step" (col. 6, lines 20-22) and particularly exemplify such sequentially conducted "binding" steps in the para. spanning cols. 8-9. Since Irsch et al failed to provide any more general direction as to how add and incubate the haptenated allergen and the magnetic microbeads, it is considered that Irsch et al have failed to point one to adding and incubating these components "simultaneously".

FINALITY

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

CONTACTS

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm and on alternate Fridays. The examiner's supervisor, Ram Shukla, can be reached on 571-272-0735. The fax number where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. For more information about the PAIR system, see http://pair-direct.uspto.gov. If you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 12/15/09 DAS

/David A Saunders/

Primary Examiner, Art Unit 1644